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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,220	09/16/2003	Shirlynn Chen	9/260	2110

28509 7590 05/04/2005

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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,220	CHEN ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-3,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-26,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/7/05;9/16/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of **Group II (claims 4-26)** in the reply filed on February 7, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant has withdrawn **claims 1-3, 27, and 28**. Applicant has presented new **claims 29 and 30**, as drawn to Group II.

The restriction is still deemed proper and made FINAL.

Claims 1-30 are pending. **Claims 4-26, 29, and 30** have been examined on the merits.

Specification

The use of the trademarks CEPLENE (page 7), VIRAMUNE, HAVRIX, AVAXIM (all on page 9), and several others (page 10) have been noted in this application. They should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

Claims 4-26, 29, and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating HCV infections, does not reasonably provide enablement for preventing HCV infections, alone or in combination with an additional therapeutic agent. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (Wands, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to treating or preventing HCV infections in a mammal via administration of compound (1), alone or in combination with an additional agent. Thus, the claims taken together with the specification imply one could prevent HCV infections in a human mammal via administration of 50 to 1000 mg of compound (1).

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The prior art recognizes the efficacy in treating HCV infections with compound (1), known in the art as BILN2061 (a.k.a. BILN 2061 or BILN-2061). The current art recognizes that it is effective in treating HCV genotype 1 (GT-1).

The art provides conflicting teachings on the efficacy of BILN2061 against GT-2 and –3. Thibeault (D. Thibeault, et al. J. Virol. (2004) 78(14), pages 7352-7359) teaches that BILN 2061, "remains a potent inhibitor of these non-genotype-1 NS3-NS4A proteins, with K_i values

below 100nM. This *in vitro* potency, in conjunction with the good pharmacokinetic data reported for humans, suggests that there is potential for BILN 2061 as an antiviral agent for individuals infected with non-genotype-1 HCV." (Abstract).

Reiser (M. Reiser, et al. Hepatology. (2005) 41(4), pages 832-835) teaches that, "the antiviral efficacy of the HCV serine protease inhibitor BILN-2061 is less pronounced and more variable in patients with HCV genotype 2 or 3 infection compared with previous results in patients with HCV genotype 1." (Abstract). Ten (10) male patients were enrolled in the study. Two (2) were administered placebo drugs, and 8 given BILN-2061. Two (2) patients with GT-2 and six (6) patients with GT-3 were given BILN-2061 (Table 1), three (3) patients had no change in viral concentrations during the study, and one (1) had a 'weak response' (Page 833, *Virological Efficacy*). Further, Reiser teaches that, "The affinity of BILN-261 for the NS3 protease of genotypes 2 and 3 has been shown to be 50 to 60 times lower than for genotype 1, therefore giving the best explanation for the overall less significant antiviral effects observed in the current study. The substantial patient-to-patient variability of antiviral responses observed in genotype 2 and 3 infections, even within the same genotype, however, can not easily be explained and are most likely the result of a complex interplay of multiple host and viral factors." "Individual differences across genotypes represent a problem for the development of the ideal anti-HCV drug, which would be active across different genotypes and prevent resistance." (Page 835).

Resier further teaches that "a cardiac histological toxicity was identified in rhesus monkeys receiving high doses of BILN-2061 for 4 weeks' duration. Boehringer Ingelheim is

continuing to evaluate various aspects of these toxicological findings and the options regarding further development of this compound." (page 835).

Pawlotsky (J.-M. Pawlotsky. J. Gastro. (2004) 127(5), pages 1629-1632) teaches that BILM 2061 was tested in 3 clinical trials, and showed, "impressive antiviral efficacy, with viral load reductions of the order of 2 to 3 log IU/mL in all patients at doses of 200 mg or more, together with excellent tolerability after 2 days treatment. Never-treated patients and nonresponsders or responder/relapsers to previous interferon-α-based therapy responded equally well to BILN 2061." "What this report does not show is the antiviral effects of BILN 2061 on genotypes other than 1, and it is noteworthy that lesser *in vitro* sensitivity of the HCV genotypes 2 and 3 proteases to BILN 2061 was recently reported. The sustainability of the antiviral response was not studied, and neither was the incidence and importance of viral resistance during longer BILN 2061 administration. Finally, this report confirms persistent rumors of cardiac toxicity with BILN 2061 in animals. This explains why no more patients have received this drug in the past 2 years, and it is hampering further human studies with longer administration." (page 1629).

Further, "BILN 2061 itself, although it has potent antiviral activity both *in vitro* and *in vivo* during short-term administration, has not entered any new clinical trials because of suspected cardiac toxicity in animals." (page 1630).

In an October 23, 2003 Press Release, Boehringer Ingelheim teaches that BILN 2061was administered to "a limited number of patients infected with HCV for two days [administration of BILN 2061] resulted in a marked reduction of the hepatitis C virus plasma levels and established the first proof-of-concept in man for an inhibitor acting by this mechanism [HCV NS3 protease

inhibition]" (page 1 of 2). "Routine chronic safety testing of high, supra-therapeutic doses in animals did, however show relevant side effects which need further analysis." "There are currently no trials ongoing with BILN 2061 and decisions about future trial swill be made after thorough evaluation of toxicity findings in animals studies." (page 1 of 2).

"Easy C Facts" (Hepatitis C Support Project, Version 1.0, April 2004, 1 page) teaches that,

> Not everyone with hepatitis C (HCV for short) has the same kind. In fact, there are six different kinds of HCV. These different kinds are called genotypes and are numbered 1 to 6. Some genotypes have further divisions called subtypes (for example, 1a and 1b)."
>
> Knowing which genotype you have is really important to your doctor because *different genotypes respond differently to treatment.* For example, genotype 1 is a little harder to treat than genotypes 2 or 3, and treating type 1 HCV requires different doses of medicine than treating types 2 or 3. [emphasis in original].

The Economist ("Needles and haystacks" October 30, 2003 *in* LiverHope (2003) 5(12), page 2 of 7) teaches that, "The bad news is that, whereas BILN2061 looked safe in early animal testing and clinical trials, further experiments in monkeys have shown that, at doses many times higher than those given to patients, the drug can throw the heart seriously out of whack." "**Boehringer Ingelheim has halted all patient testing with BILN2061**, and has returned to the drawing board to work out why BILN2061 has this effect." [emphasis in original].

The Cleveland Clinic (Hepatitis C Management "Future Directions in Hepatitis C Therapy, accessed 4/18/05, 2 pages) teaches that, "despite substantial advances in the treatment

of chronic HCV infection, many unmet needs remain, prompting further evolution of therapeutic approaches." (page 1 of 2). "Further testing of BILN 2061 is on hold because of histological evidence of cardiovascular toxicity in monkeys given the drug for 4 weeks." (page 2 of 2).

Treatment of HCV GT-1, -2, and –3 infections with pegylated interferon and ribavirin (a.k.a. ribavarin) is known in the art (e.g., J.G. McHutchison, et al. N. Engl. J. Med. (1998), 339, pages 1485-1492; M.P. Manns, et al. Lancet (2001), 358, pages 958-965).

The art is silent to prevention of HCV infections with BILN-2061, in the current or prior art. It is noted that the references citing toxicity in the monkey model do not teach a specific dose administered.

The instant claims also encompass using the claimed compound to prevent HCV infections which is clearly beyond the scope of the instantly disclosed/claimed invention. Please note that the term "prevent" is an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does "therapeutic" or "treat", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes) – including preventing such disorders as HCV infections, which is clearly not recognized in the medical art as being a totally preventable condition.

Since the ability to prevent HCV infections remains largely unsolved, the compound, BILN 2061, is of questionable toxicity, and unpredictable in treating HCV infections, and has not advanced beyond the 'testing' of the compound, means for prevention of HCV infections is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided examples of generating pharmaceutical compositions comprising compound (1), how to generate a 8.33 mg/mL, 66.7 mg/mL, and 166.7mg/mL solution, and how to administer the solution orally. Furthermore, the specification asserts that, "Compound (1) administered in an oral pharmaceutical at a selected dosage range was highly effective at reducing the viral load of HCV infected patients." (page 3).

However, the specification does not provide examples, working or prophetic, correlating the doses administered and the response elicited, as instantly claimed, in any subject *in vitro* or *in vivo*.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the toxicity of the compound, the high unpredictability, with regards to efficacy of BILN 2061, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to prevent HCV with compound (1), alone or in combination with another therapeutic agent.

It is the Examiner's position that one skilled in the art could not practice the invention commensurate in the scope of the claims without undue experimentation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-26, 29, and 30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 143-145 of U.S. Patent No. 6,608,027 B1 ('027) or over claims 35 and 77 of U.S. Patent No. 6,828,301 B2 ('301); each in view of McHutchinson, *supra.*

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims, and those of '027 are both drawn to methods of preventing and treating hepatitis C viral (HCV) infections, alone or in combination with another agent (e.g., ribavirin), and administered in a pharmaceutical preparation, wherein the instantly used compound (1), is a specifically claimed embodiment, though not specifically used in the methods.

'027 teaches compound (1) as '822' (claim 108). It is in a pharmaceutical composition in admixture with a pharmaceutically acceptable carrier medium or auxiliary agent (claim 115), wherein the pharmaceutical further comprises α-interferon (claim 118) and/or ribavirin (claims 120, 124).

'027 does not specifically teach pegylated interferon, the instantly claimed dosages, PEG:EtOH as the solvent, the instantly claimed viral load reduction, treating genotype 1 of HCV, or the dose regimen.

'301 teaches a method of treating hepatitis C viral infections in a mammal via administration of a therapeutically effective amount of a compound of the genus from which 822 is a member. 822 is a specifically claimed embodiment of a pharmaceutical composition (claim 25). Looking to the specification to define preferred embodiments of the composition, it is noted that formulation #4 comprises 822, ethanol and PEG.

'301 does not teach ribavirin, and/or pegylated interferon, the instantly claimed dosages, the instantly claimed viral load reduction, treating genotype 1 of HCV, or the dose regimen.

With regards to '027, it would have been obvious to use 822 in the methods, alone or in combination with ribavirin, as it is a claimed embodiment of the compounds and pharmaceutical compositions. One would have been motivated to use any of the compounds, including 822, in the methods, alone or in combination, because it is a specifically claimed embodiment of the compounds and pharmaceutical compositions. One would have a high expectation for success in the methods, as the specification of '027 teaches that 822 has an EC_{50} of ≤ 1 μM in cellular assays, and is a specifically claimed embodiment of the genus from which it depends.

With regards to '301, it would have been obvious to use 822 in the methods as it is a claimed embodiment of the genus of pharmaceutical compositions used in the methods, and it is a preferred embodiment of formulations.

With regards to the dose regimen/ dose administered, it would have been obvious to one skilled in the art at the time of invention to determine all operable and optimum dosages and

administration regimens, in the claimed method of '027 or '301, because dosages and administration regimens are an art-recognized result-effective variable that is routinely determined and optimized in the formulary and pharmaceutical arts.

With regards to the viral load reduction, as instantly claimed, administration of the compound would intrinsically provide the asserted benefit when administered to a mammal., as it is a biological response to the drug administration, and is not a variable of the method of administration *per se*.

With regards to GT-1, it would have been obvious to administer it to all patients, including GT-1, as the patient populations of '027 and/or '301 do not preclude administration to any one genotype of HCV. One would have a reasonable expectation for success in treating GT-1 with 822, as it is a claimed embodiment of a pharmaceutical for treating HCV.

With regards to the solvent PEG:EtOH, if not expressly taught by '027, based upon the overall beneficial teaching provided by this reference with respect to treating and/ or preventing HCV infections with the genus encompassing 822, the adjustments of particular conventional working conditions (e.g., determining one or more suitable solvents in which 822 is soluble in), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

With regards to pegylated interferon, as taught by McHutchinson, *supra*, pegylated-α-interferon and ribavirin in combination are known in the art for treating HCV infections.

As set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980), "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose

in order to form third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art."

Because both compositions are taught in the art for treating HCV infections, it would have been obvious to combine both for the benefit of making, and using, a composition which is useful for treating HCV infections.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 4, 5, 8-12, and 22-24 are rejected under 35 U.S.C. 102(e) as being anticipated by '301

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The instant claims are presented *supra*. The teachings of '301 are presented *supra*.

'301 teaches administration of 100 mg of 822 to beagle dogs (column 42, line 21+) and administration of 822 to monkeys at 40 mg/kg (column 41, line 44+). The composition is administered in a PEG:EtOH mixture to the beagle dogs. With regards to the alleged biological effects, e.g.- lower HCV viral load, because the art teaches administration of the compound, it is considered inherent to the method. Further, because the art does not exclude administration to any HCV genotype, and because there are so few genotypes of HCV, the method of administration to treat HCV necessarily treats HCV GT-1 infections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-26, 29 and 30 are rejected under 35 U.S.C. 103(a) as being obvious over '301, as applied to claims 4, 5, 8-12, and 22-24, *supra*; or over '027, each in view of McHutchinson.

The applied references have a common assignee with the instant application. Based upon the earlier effective U.S. filing dates of the references, each constitutes prior art only under 35 U.S.C. 102(e).

This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in

the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The instant claims are presented *supra*.

The teachings of '027, '301 and McHutchinson are presented *supra*.

With regards to '027, it would have been obvious to use 822 in the methods, alone or in combination with ribavirin, as it is a claimed embodiment of the compounds and pharmaceutical compositions. One would have been motivated to use any of the compounds, including 822, in the methods, alone or in combination, because it is a specifically claimed embodiment of the compounds and pharmaceutical compositions. One would have a high expectation for success in the methods, as the specification of '027 teaches that 822 has an EC_{50} of ≤ 1 μM in cellular assays, and is a specifically claimed embodiment of the genus from which it depends.

With regards to '301, it would have been obvious to use 822 in the methods as it is a claimed embodiment of the genus of pharmaceutical compositions used in the methods, and it is a preferred embodiment of formulations, and is administered to beagles and monkeys, as presented *supra*.

With regards to the dose regimen/ dose administered, it would have been obvious to one skilled in the art at the time of invention to determine all operable and optimum dosages and administration regimens, in the claimed method of '027 or '301, because dosages and administration regimens are an art-recognized result-effective variable that is routinely determined and optimized in the formulary and pharmaceutical arts.

With regards to the viral load reduction, as instantly claimed, administration of the compound would intrinsically provide the asserted benefit when administered to a mammal., as it

is a biological response to the drug administration, and is not a variable of the method of administration *per se*.

With regards to GT-1, it would have been obvious to administer it to all patients, including GT-1, as the patient populations of '027 and/or '301 do not preclude administration to any one genotype of HCV. One would have a reasonable expectation for success in treating GT-1 with 822, as it is a claimed embodiment of a pharmaceutical for treating HCV.

With regards to the solvent PEG:EtOH, if not expressly taught by '027, based upon the overall beneficial teaching provided by this reference with respect to treating and/ or preventing HCV infections with the genus encompassing 822, the adjustments of particular conventional working conditions (e.g., determining one or more suitable solvents in which 822 is soluble in), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

With regards to pegylated interferon, as taught by McHutchinson, *supra*, pegylated-α-interferon and ribavirin in combination are known in the art for treating HCV infections.

As set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980), "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art."

Because both compositions are taught in the art for treating HCV infections, it would have been obvious to combine both for the benefit of making, and using, a composition which is useful for treating HCV infections.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

NO CLAIMS ARE ALLOWED.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Andrew D. Kosar, Ph.D.
Patent Examiner
Art Unit 1654

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